

REMARKS

Applicant submits this Amendment to indicate the insertion point for the Sequence Listing filed concurrently herewith. Application respectfully requests examination on the merits of this application.

Respectfully submitted,

By _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Marked up replacementTables:

Table 3

		FRI	CDRI	FR2
		1	3	4
		12345678901234567890123	45678901234	567890123456789
AHM	(SEQ ID NO: 130)	DIVMTQSHKFMSTSVGDRVSITC	KASQDVNTAVA	WYQQKPGQSPKLLIY
HuSG	I (SEQ ID NO: 131)	DIQMTQSPSSLSASVGDRVTITC		WYQQKPGKAPKLLIY
REI	(SEQ ID NO: 132)	DIQMTQSPSSLSASVGDRVTITC		WYQQKPGKAPKLLIY
RVLa	(SEQ ID NO: 133)	-----	-----	-----
RVLb	(SEQ ID NO: 134)	-----	-----	-----

		CDR2	FR3	
		5	6	7
		0123456	7890123456789012345678	8
AHM	(SEQ ID NO: 130)	SASNRYT	GVPDRITGSGSGTDFTFTISSVQAEDLALYYC	
HuSG	I (SEQ ID NO: 131)		GVPSRFSGSGSGTDFTLTISLQPEDFATYYC	
REI	(SEQ ID NO: 132)		GVPSRFSGSGSGTDFTFTISSLQPEDIATYYC	
RVLa	(SEQ ID NO: 133)	-----	-----	-----
RVLb	(SEQ ID NO: 134)	-----	-----Y-----	-----

		CDR3	FR4	
		9	10	
		901234567	8901234567	
AHM	(SEQ ID NO: 130)	QQHYSTPFT	FGSGTKLEIK	
HuSG	I (SEQ ID NO: 131)		FGQGTKVEIK	
REI	(SEQ ID NO: 132)		FGQGTKVEIK	
RVLa	(SEQ ID NO: 133)	-----	-----	
RVLb	(SEQ ID NO: 134)	-----	-----	

Table 4

		FRI	CDR1	FR2
		1	3	4
		123456789012345678901234567890	12345	67890123456789
AHM	(SEQ ID NO: 135)	QVQLQSGAELARPGASVKLSCKASGYTFT	PYWMQ	WVKQRPGQGLEWIG
HuSGI	(SEQ ID NO: 136)	EVQLVQSGADVKKPGXSXVVSCKASGYTFS		WVRQAPGXGLDWVG
HG3	(SEQ ID NO: 137)	QVQLVQSGAEVKKPGASVKVSCKASGYTFN		WVRQAPGQGLEWMG
RVHa	(SEQ ID NO: 138)	-----T	-----	-----
RVHb	(SEQ ID NO: 139)	-----T	-----	-----
RVHc	(SEQ ID NO: 140)	-----T	-----	-----
RVHd	(SEQ ID NO: 141)	-----T	-----	-----
RVHe	(SEQ ID NO: 142)	-----T	-----	-----
RVHf	(SEQ ID NO: 143)	-----T	-----	-----
RVHg	(SEQ ID NO: 144)	-----T	-----	-----R-----
RVHh	(SEQ ID NO: 145)	-----T	-----	-----
RVHi	(SEQ ID NO: 146)	-----T	-----	-----
RVHj	(SEQ ID NO: 147)	-----T	-----	-----
RVHk	(SEQ ID NO: 148)	-----T	-----	-----
RVHl	(SEQ ID NO: 149)	-----T	-----	-----
RVHm	(SEQ ID NO: 150)	-----T	-----	-----
RVHn	(SEQ ID NO: 151)	-----T	-----	-----

RVHo	(SEQ ID NO: 152)	-----T	-----	-----
RVHp	(SEQ ID NO: 153)	-----T	-----	-----
RVHq	(SEQ ID NO: 154)	-----T	-----	-----
RVHr	(SEQ ID NO: 155)	-----T	-----	-----

Table 5

	CDR2	FR3	
	5 6 7 8 9	7 8 9	
AHM	(SEQ ID NO: 156)	012A3456789012345	67890123456789012ABC345678901234
HuSGI	(SEQ ID NO: 157)	SIFPGDGDTRYSQKFKG	KATLTADKSSSTAYMQLSILAFEDSAVYYCAR
HG3	(SEQ ID NO: 158)		RVTXTXDXSXNTAYMELSSLRSED TAVYYCAR
RVHa	(SEQ ID NO: 159)	-----	-----A-----
RVHb	(SEQ ID NO: 160)	-----	K-----A-----
RVHc	(SEQ ID NO: 161)	-----	-----A-K-----
RVHd	(SEQ ID NO: 162)	-----	K-----A-K-----
RVHe	(SEQ ID NO: 163)	-----	-A-L-A-----
RVHf	(SEQ ID NO: 164)	-----	-A-L-A---S--A-----
RVHg	(SEQ ID NO: 165)	-----	-----A-----
RVHh	(SEQ ID NO: 166)	-----	K-----A---S--A-----
RVHi	(SEQ ID NO: 167)	-----	K-----A---S--A-----AF-----
RVHj	(SEQ ID NO: 168)	-----	KA-L-A---S--A-----
RVHk	(SEQ ID NO: 169)	-----	K-----A---S==A--Q-----
RVHl	(SEQ ID NO: 170)	-----	K-----A---S--A--Q--1-----
RVHm	(SEQ ID NO: 171)	-----	K-----A---S--A--Q--1-----S-----
RVHn	(SEQ ID NO: 172)	-----	K-----A---S--A-----1-----
RVHo	(SEQ ID NO: 173)	-----	K-----A---S--A-----S-----
RVHp	(SEQ ID NO: 174)	-----	-----A-----A-----
RVHq	(SEQ ID NO: 175)	-----	-----A---S-----
RVHr	(SEQ ID NO: 176)	-----	-----A-K---A-----

Table 6

	CDR3	FR4	
	10 11	11	
AHM	(SEQ ID NO: 177)	57890ABJK12	34567890123
HuSGI	(SEQ ID NO: 178)	GLRRGGYYFDY	WGQGTTLTVSS
HG3	(SEQ ID NO: 179)	-----	WGQGTTLTVSS
RVHa	(SEQ ID NO: 180)	-----	WGQGTTLTVSS
RVHb	(SEQ ID NO: 181)	-----	-----
RVHc	(SEQ ID NO: 182)	-----	-----
RVHd	(SEQ ID NO: 183)	-----	-----
RVHe	(SEQ ID NO: 184)	-----	-----
RVHf	(SEQ ID NO: 185)	-----	-----
RVHg	(SEQ ID NO: 186)	-----	-----
RVHh	(SEQ ID NO: 187)	-----	-----
RVHi	(SEQ ID NO: 188)	-----	-----
RVHj	(SEQ ID NO: 189)	-----	-----
RVHk	(SEQ ID NO: 190)	-----	-----
RVHl	(SEQ ID NO: 191)	-----	-----
RVHm	(SEQ ID NO: 192)	-----	-----
RVHn	(SEQ ID NO: 193)	-----	-----
RVHo	(SEQ ID NO: 194)	-----	-----
RVHp	(SEQ ID NO: 195)	-----	-----
RVHq	(SEQ ID NO: 196)	-----	-----
RVHr	(SEQ ID NO: 197)	-----	-----

Design of V region of Natural Humanized Antibody

A) L chain

	FRI	1	2	CDR1	3	FR2	4	CDR2	5
HM1.24 (SEQ ID NO: 130)	12345678901234567890123			45678901234		567890123456789		0123456	
HuSg I (SEQ ID NO: 131)	DIQMTQSPSSLSASVGDRTITC			KASQDVNTAVA		WYQQKPGQSPKLLIY		SASNRYT	
REI (SEQ ID NO: 132)	DIQMTQSPSSLSASVGDRTITC					WYQQKPGKAPKLLIY			
Primary design (RVLa (SEQ ID NO: 133))	-----			-----		-----		-----	
Secondary design (SEQ ID NO: 133)	-----			-----		-----		-----	

FR3
6

FR2
10

	7	8	9	CDR1	10
78901234567890123456789012345678				901234567VA	8901234567
GVPDRITGSGSGTDFTTISSVQAEALAIYC				QOHYSTPFT	FGSGTKLEIK
GVPSRFSGSGGTDFLTITSSLPEDFATYYC					FGQGTKVEIK
GVPSRFSGSGGTDFLTITSSLPEDFATYYC					FGQGTKVEIK

HM1.24 (SEQ ID NO: 130)
 HuSg I (SEQ ID NO: 131)
 REI (SEQ ID NO: 132)
 Primary design (RVLa (SEQ ID NO: 133))
 Secondary design (SEQ ID NO: 133)

B) H chain

Design of V region of Natural Humanized Antibody

	FR1	1	2	3	CDR1	4	FR2	5	6
HM1.24 (SEQ ID NO: 198)	123456789012345678901234567890				12345	67890123456789		01234567890	
HuSg I (SEQ ID NO: 199)	QVQLQSGAEELARPGASVKLSCKASGYTFT				PYWMQ	WVKQRPQGLEWIG		SIFPGDGYTRYSQKFKG	
HG3 (SEQ ID NO: 200)	EVQLVQSGADVKKPGXSVXVSKASGYTFS					WVRQAPGGLDWVG			
Primary design (RVHr (SEQ ID NO: 201))	QVQLVQSGAEVKKPGASVKVSKASGYTFN					WVRQAPGQGLEWMG			
Secondary design (2NDRvh) (SEQ ID NO: 202)	-----T				-----T	-----		-----	

FR3
7

FR2
11

	8	9	10	CDR3	11
67890123456789012345678901234				57890ABJK12	34567890123
KATLTADKSSSTAYMQLSILAFDSAVYYCAR				GLRRGGYYFDY	WGQGTTLTVSS
RVXTXDXSXNTAYNELSSLRSEDTAVYYCAR					WGQGTTLTVTVSS

Atty. Dkt. No. 053466/0274

WGQGTTVTVSS

RVTMTRDTSTSTVIMELSSLRSED TAVYICAR

Primary design (RVLa/Hr)
Secondary design (2nd RVH)

-----A-K-----A-----
---I-A-K---A-----

Marked up page 74 line 23.

FR3 of primary design antibody (SEQ ID NO: 203)